

WHAT WE CLAIM IS:

1. A method of inducing an immune response comprising:  
(a) applying a formulation to intact skin of an organism, wherein the formulation comprises an antigen and an adjuvant;  
(b) activating a Langerhans cell with the adjuvant; and  
(c) presenting the antigen on a cell surface of the Langerhans cell to a lymphocyte, thereby inducing the immune response in the organism.

2. The method of claim 1, wherein the formulation consists essentially of antigen and adjuvant.

3. The method of claim 1, wherein the formulation further comprises liposomes.

4. The method of claim 1, wherein a physical, chemical, electrical, or sonic penetration enhancer.

5. The method of claim 1, wherein the immune response is not an allergic reaction.

6. The method of claim 1 further comprising applying alcohol to the intact skin prior to application of the formulation.

7. The method of claim 1, wherein the immune response comprises an antigen-specific lymphocyte.

8. The method of claim 7, wherein the immune response comprises generation of an antigen-specific B cell.

9. The method of claim 8, wherein the immune response further comprises an antigen-specific antibody.

10. The method of claim 1, wherein the antigen has a molecular weight greater than 500 daltons.

11. The method of claim 1, wherein the antigen is derived from a source selected from the group consisting of a pathogen, a tumor cell, or a normal cell.

12. The method of claim 1, wherein the antigen is derived from a pathogen selected from the group consisting of bacterium, virus, fungus, and parasite.

13. The method of claim 1, wherein the antigen is a tumor antigen or an autoantigen.

14. The method of claim 1, wherein the antigen is selected from the group consisting of carbohydrate, glycolipid, glycoprotein, lipid, lipoprotein, phospholipid, and polypeptide.

15. The method of claim 1, wherein the formulation comprises an attenuated live virus and the antigen is expressed by the attenuated live virus.

16. The method of claim 1, wherein the antigen is a polypeptide of greater than 500 daltons molecular weight.

17. The method of claim 1, wherein the antigen is multivalent.

18. The method of claim 1 further comprising activating the Langerhans cell to increase major histocompatibility complex class II expression.

19. The method of claim 1 further comprising the Langerhans cell migrating to a lymph node of the organism.

20. The method of claim 1, wherein the adjuvant activates the Langerhans cell.

21. The method of claim 1, wherein the adjuvant enhances antigen presentation to a lymphocyte.

22. The method of claim 1, wherein the adjuvant is an ADP-ribosylating exotoxin.

23. The method of claim 22, wherein the adjuvant is cholera toxin (CT) or cholera toxin B subunit (CTB).

24. The method of claim 22, wherein the adjuvant is *E. coli* heat-labile enterotoxin (LT) or pertussis toxin.

25. The method of claim 22, wherein the adjuvant in the formulation is provided as a nucleic acid encoding an ADP-ribosylating exotoxin.

26. The method of claim 1, wherein the antigen in the formulation is provided as a nucleic acid encoding the antigen.

27. The method of claim 1, wherein the formulation is a gel or emulsion or ointment.

28. The method of claim 1, wherein the formulation is applied with an occlusive dressing.

29. The method of claim 1, wherein the formulation is applied to intact skin covering more than one draining lymph node field.

30. A method of immunization comprising applying a formulation to intact skin of an organism, wherein the formulation comprises an antigen and an adjuvant.

31. A method of inducing an immune response comprising:  
(a) applying a formulation to intact skin of an organism, wherein the formulation comprises an antigen and an ADP-ribosylating exotoxin; and

Sub 89  
DE (b) inducing the immune response in the organism without perforating the skin, wherein the immune response is specific for the antigen.

---

32. A method of inducing an immune response comprising:  
(a) applying a formulation to intact skin of an organism, wherein the formulation comprises an antigen and an adjuvant;

Sub 89  
PLP (b) activating an antigen presenting cell with the adjuvant; and

(c) presenting the antigen on a cell surface of the antigen presenting cell to a lymphocyte, thereby inducing the immune response in the organism.

---

33. A method of inducing an immune response comprising:  
(a) applying an antigen epicutaneously on an organism,  
(b) activating a Langerhans cell underlying the skin with an ADP-ribosylating exotoxin,

(c) signaling the Langerhans cell to migrate to a lymph node of the organism and mature into a dendritic cell, and

(d) presenting the antigen on a cell surface of the dendritic cell to a lymphocyte; thereby inducing the immune response in the organism, wherein the immune response is specific for the antigen.

---

34. The method of claim 33, wherein the dendritic cell presents antigen in a T-cell region.

35. The method of claim 33, wherein the dendritic cell presents antigen in a B-cell follicle.

---

36. A method of inducing an immune response to an antigen comprising:

Sub 89  
A6 (a) applying a formulation to intact skin of an organism, wherein the formulation comprises (i) a nucleic acid containing a sequence encoding the antigen and (ii) an adjuvant; and

(b) inducing the immune response in the organism without perforating the skin, wherein the immune response is specific for the antigen.

37. The method of claim 36, wherein the formulation consists essentially of nucleic acid and adjuvant.

38. The method of claim 36, wherein the formulation does not include a penetration enhancer, viral particle, liposome, or charged lipid.

39. The method of claim 36, wherein the nucleic acid is non-integrating and non-infectious.

40. The method of claim 36, wherein the nucleic acid further contains a regulatory region operably linked to the sequence encoding the antigen.

41. A patch for transcutaneous immunization comprising:

- (a) a dressing,
- (b) an antigen, and
- (c) an adjuvant; whereby application of the patch to intact skin induces an immune response specific for the antigen.

42. The patch of claim 41, wherein the dressing is an occlusive dressing.

43. The patch of claim 41, wherein exposure of a Langerhans cell to the adjuvant activates the Langerhans cell.

44. The patch of claim 41, wherein exposure of a Langerhans cell to the adjuvant causes migration of the Langerhans cell to a lymph node.

45. The patch of claim 41, wherein exposure of a Langerhans cell to the adjuvant signals the Langerhans cell to mature into a dendritic cell.

46. The patch of claim 41, wherein the adjuvant is an ADP-ribosylating exotoxin.

47. The patch of claim 46, wherein the adjuvant is cholera toxin (CT) or cholera toxin B subunit (CTB).

48. The patch of claim 46, wherein the adjuvant is *E. coli* heat-labile enterotoxin (LT) or pertussis toxin.

49. The patch of claim 41, wherein the patch covers more than one draining lymph node field.

add  
p12

add D11